

## **REMARKS**

### **Introduction:**

Claims 30-41 are pending in the present application. Applicants are amending herewith Claims 32-34 and 38-41. Applicants submit that the present amendments should be entered because they place the claims in condition for allowance and/or place the claims in better condition for appeal. Applicants further submit that the foregoing amendments do not narrow the scope of the claims, but, rather, merely clarify those limitations already present. Following entry of the present amendments, Claims 30-41 will be pending and subject to examination.

### **The Office Action:**

Claims 30-41 were rejected under 35 U.S.C. § 112, first paragraph, as not being enabling for inhibition of neovascularization. Claims 30, 32, 33, 35, 36, 38, 39 and 41 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting in view of Claims 46-62 of co-pending application Serial No. 10/280,831. Claims 30-41 were rejected under the judicially created doctrine of obviousness-type double patenting in view of U.S. Patent Nos. 5,504,074 and 5,661,143. Claims 30, 35, 36 and 41 were rejected under 35 U.S.C. § 102(b) as being anticipated and unpatentable over the publication by Seegers et al. Claims 31-34 and 37-40 were rejected under 35 U.S.C. § 103(a) as being obvious and unpatentable over the published article by Seegers et al. Applicants respectfully traverse the foregoing rejections.

### **The Rejections Under 35 U.S.C. § 112:**

Claims 30-41 were rejected under 35 U.S.C. § 112, first paragraph, as not reasonably providing enablement for inhibition of neovascularization not due to angiogenesis.

The rejection previously stated that the claimed compounds have anti-mitotic activity that was “evaluated by testing their ability to inhibit the proliferation of new blood vessel cells (angiogenesis).” The rejection previously defined angiogenesis as the process of neovascularization from pre-existing blood vessels. The rejection previously stated that the term neovascularization is broader than angiogenesis and includes proliferation of blood vessels in tissue not normally containing them or proliferation of blood vessels of a different kind than usual in a tissue. The rejection previously concluded that the present specification lacks examples of proliferation of blood vessels in tissue not normally containing them or of a different kind than usual in a tissue, and, thus, does not provide guidance to enable the skilled artisan to practice the claimed invention commensurate in scope with the instant claims. Applicants respectfully disagree.

Nevertheless, in the present Office Action, the examiner states that applicants’ previous argument is that all neovascularization in humans or animals is associated with angiogenesis. The examiner then suggests that if such is the case, applicants’ substitution of the term angiogenesis for neovascularization would overcome the present rejection. In response to the statement by the examiner, applicants are amending the claims herewith to substitute the term angiogenesis for the term neovascularization. Since applicants have complied with the examiner’s suggestion, applicants submit that Claims 30-41 are not indefinite under 35 U.S.C. § 112, first paragraph, and, therefore, the rejection on that basis should be withdrawn. Applicants further submit that the amendment of the claims, as stated above, do not narrow the scope of the claims.

**The Double Patenting Rejections:**

Claims 30, 32, 33, 35, 36, 38, 39 and 41 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting in view of the claims of co-pending application Serial No. 10/280,831. Since this is a provisional rejection, applicants submit that no response is due.

Claims 30-41 were rejected under the judicially created doctrine of obviousness-type double patenting in view of U.S. Patent Nos. 5,504,074 and 5,661,143. Accordingly, applicants are submitting herewith a terminal disclaimer with respect to U.S. Patent Nos. 5,504,074 and 5,661,143 in compliance with 37 CFR 1.321. Applicants are also submitting herewith the fee required by 37 CFR 1.20(d). Applicants submit that the filing of the terminal disclaimer overcomes the present rejection. Accordingly, applicants respectfully request that the rejection of Claims 30-41 on the basis of obviousness-type double patenting in view of U.S. Patent Nos. 5,504,074 and 5,661,143 be withdrawn.

**The Rejection Under 35 U.S.C. § 102:**

Claims 30, 35, 36 and 41 were rejected under 35 U.S.C. § 102(b) as being anticipated and unpatentable over the article by Seegers et al. The rejection states that Seegers et al. teaches the antimitotic properties of 2-methoxyestradiol. Applicants respectfully disagree.

Applicants' previous arguments regarding Seegers et al. are incorporated herein by reference. Additionally, however, the present invention is directed to the treatment of ocular angiogenesis. Angiogenesis is the formation of new or additional blood vessels from preexisting blood vessels. These new blood vessels are formed from endothelial cells. The only cells tested by Seegers et al. were dividing MFC-7 and HeLa cells. Those cells have no relation to the

endothelial cells associated with angiogenesis, which is the subject of the present invention. The present invention is useful to treat the diseases that are the subject of the present claims by inhibiting angiogenesis, that is inhibiting the growth of endothelial cells. Applicants are amending herewith Claims 32-34 and 38-41 to more clearly point out that the diseases that are the subject of the claims are treated by administering an effective **angiogenesis-inhibiting** amount of a composition comprising 2-methoxyestradiol. There is no disclosure or suggestion whatsoever in Seegers et al. of inhibiting angiogenesis to treat the diseases that are the subject of the present claims, such as ocular neovascularization.

In order for the Seegers et al. paper to anticipate the presently claimed invention, Seegers et al. must disclose each and every element of the claimed invention. Since the Seegers et al. paper does not disclose the use of 2-methoxyestradiol to treat endothelial cells or ocular angiogenesis, applicants submit that the rejection of Claims 30, 35, 36 and 41 under 35 U.S.C. § 102(b) as being anticipated and unpatentable in view of the publication by Seegers et al. is improper and should be withdrawn.

**The Rejection Under 35 U.S.C. § 103:**

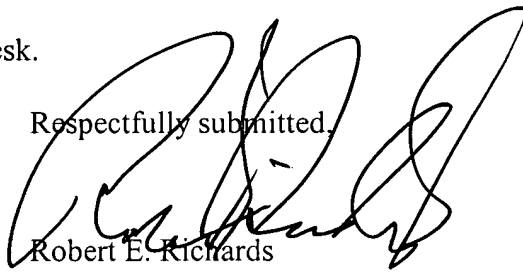
Claims 31-34 and 37-40 were rejected under 35 U.S.C. § 103(a) as being obvious and unpatentable over the article by Seegers et al. The rejection previously stated that Seegers et al. teaches the anti-mitotic properties of 2-methoxyestradiol. The rejection further previously stated that the instant claims differ from the reference by reciting inhibition of ocular neovascularization. The rejection previously concluded that the ordinary artisan would have reasonably expected that 2-methoxyestradiol would inhibit cell mitosis in any tissue, including ocular tissue. Applicants respectfully disagree.

Rather than restating the same arguments as set forth above regarding the rejection under 35 U.S.C. § 102, applicants incorporate herein by reference those same arguments. Claims 31-34 and 37-40 relate to compounds other than 2-methoxyestradiol or to the treatment of ocular neovascularization. Seegers et al. neither discloses or suggests these other estradiol derivatives or the treatment of ocular neovascularization. Accordingly, applicants submit that the rejection of Claims 31-34 and 37-40 under 35 U.S.C. § 103(a) as being obvious and unpatentable in view of the publication by Seegers et al. is improper and should be withdrawn.

**Conclusion:**

Applicants respectfully request reconsideration of the present application in view of the foregoing remarks and amendment. Such action is courteously solicited. Applicants submit that all claims are now in condition for allowance. Applicants hereby request a telephone interview with the examiner. Accordingly, applicants request that the examiner call the undersigned when this response reaches her desk.

Respectfully submitted,



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